

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
16 June 2005 (16.06.2005)

PCT

(10) International Publication Number
WO 2005/053600 A3

(51) International Patent Classification: **C12N 15/11,**
A61K 31/7088, A61P 25/00, 27/02

(21) International Application Number:
PCT/IB2004/004431

(22) International Filing Date:
3 December 2004 (03.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
529936 3 December 2003 (03.12.2003) NZ

(71) Applicant (for all designated States except US): CODA
THERAPEUTICS (NZ) LTD [NZ/NZ]; 3/4 Crescent
Road, Epsom, Auckland (NZ).

(71) Applicants (for US only): LAUX, Wilda [NZ/NZ]; 33A
Secoia Crescent, Mangere (NZ). GREEN, Collin, R.
[NZ/NZ]; 3/4 Crescent Road, Epsom, Auckland (NZ).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii)) for the following designations AE,

AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM,
ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA,
SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR),
OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii)) for the following designa-
tions AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW,
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ,
EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA,
ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ,
NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT,
BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG)

— of inventorship (Rule 4.17(iv)) for US only

Published:

— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
2 March 2006

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: ANTISENSE COMPOUNDS TARGETED TO CONNEXINS AND METHODS OF USE THEREOF

(57) Abstract: Methods and compositions for modulating the activities of connexins are provided, including, for example, for use in post-surgical, trauma, or tissue engineering applications. These compounds and methods can be used therapeutically, for example, to reduce the severity of adverse effects associated diseases and disorders where localized disruption in direct cell-cell communication is desirable.

INTERNATIONAL SEARCH REPORT

Intern: I Application No
PCT/IB2004/004431

A. CLASSIFICATION OF SUBJECT MATTER

C12N15/11 A61K31/7088 A61P25/00 A61P27/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/44409 A (UNIVERSITY COLLEGE LONDON; BECKER, DAVID, LAURENCE; GREEN, COLIN, RICH) 3 August 2000 (2000-08-03) cited in the application	1-5, 57-63, 65,67,68
Y	the whole document	1-56,67, 68
X	BECKER DAVID L ET AL: "Connexin alpha1 and cell proliferation in the developing chick retina" EXPERIMENTAL NEUROLOGY, vol. 156, no. 2, April 1999 (1999-04), pages 326-332, XP002347187 ISSN: 0014-4886	1,2,5, 67,68
Y	the whole document	1-56,67, 68
----- -/--		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T", later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "B" document member of the same patent family

Date of the actual completion of the international search

29 September 2005

Date of mailing of the international search report

03 JAN 2006

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Andres, S

INTERNATIONAL SEARCH REPORT

Intern 31 Application No
PCT/IB2004/004431

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>GREEN, C. ET AL.: "Spatiotemporal depletion of connexins using antisense oligonucleotides." METHODS IN MOLECULAR BIOLOGY (CLIFTON, N.J.) 2001, vol. 154, 2001, pages 175-185, XP008053224 ISSN: 1064-3745 cited in the application the whole document</p> <p>-----</p>	57-65
X	<p>FRANTSEVA MARINA V ET AL: "Ischemia-induced brain damage depends on specific gap-junctional coupling" JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM, vol. 22, no. 4, April 2002 (2002-04), pages 453-462, XP008053227 ISSN: 0271-678X the whole document</p> <p>-----</p>	57-65
A	<p>RATKAY-TRAUB I ET AL: "Regeneration of rabbit cornea following excimer laser photorefractive keratectomy: A study on gap junctions, epithelial junctions and epidermal growth factor receptor expression in correlation with cell proliferation" EXPERIMENTAL EYE RESEARCH, vol. 73, no. 3, September 2001 (2001-09), pages 291-302, XP002347188 ISSN: 0014-4835 the whole document</p> <p>-----</p>	1-65,67, 68
A	<p>QIU C ET AL: "Targeting Connexin43 Expression Accelerates the Rate of Wound Repair" CURRENT BIOLOGY, vol. 13, no. 19, 30 September 2003 (2003-09-30), pages 1697-1703 - S1, XP004545249 ISSN: 0960-9822 cited in the application the whole document, especially page S1</p> <p>-----</p>	1-65,67, 68
A	<p>BALDWIN HEATHER C ET AL: "Growth factors in corneal wound healing following refractive surgery: A review" ACTA OPHTHALMOLOGICA SCANDINAVICA, vol. 80, no. 3, June 2002 (2002-06), pages 238-247, XP002347189 ISSN: 1395-3907 cited in the application the whole document</p> <p>-----</p>	24-26
	-/--	

INTERNATIONAL SEARCH REPORT

Intern: 1 Application No
PCT/IB2004/004431

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WILLECKE KLAUS ET AL: "Structural and functional diversity of connexin genes in the mouse and human genome" BIOLOGICAL CHEMISTRY, vol. 383, no. 5, May 2002 (2002-05), pages 725-737, XP008053223 ISSN: 1431-6730 cited in the application</p> <p>-----</p>	
A	<p>SANTORDO S W ET AL: "A GENERAL PURPOSE RNA-CLEAVING DNA ENZYME" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 94, April 1997 (1997-04), pages 4262-4266, XP001009844 ISSN: 0027-8424 cited in the application</p> <p>-----</p>	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2004/004431

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-65 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Invention 1.: claims 1-64, 67, 68 (all partially) and claim 65

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1.: claims 1-64,67,68 (all partially) and claim 65

Use of antisense oligonucleotides against SEQ ID 12 (connexin 43) in methods for enhancing healing of wounds associated with surgical procedures on the eye or the central nervous system.

Inventions 2. to 4.: Claims 1-64,67,68 (all partially)

As for subject 1., but concerning the connexins 26 (SEQ ID 22), 37 (SEQ ID 14) and 30 (SEQ ID 26) respectively.

Invention 5.: Claims 1-64,67-68 (all partially) and claim 66

As for subject 1., but concerning connexin 31.1 (SEQ ID 25).

Inventions 6. to 19.: Claims 1-6,9-14,16-64,67,68 (all partially)

As for subject 1., but concerning the connexins defined by SEQ IDs 13, 15-21, 23, 24 and 27-31 respectively.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern. Application No
PCT/IB2004/004431

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0044409	A	03-08-2000	
		AT 300959 T	15-08-2005
		AU 776512 B2	09-09-2004
		AU 2119300 A	18-08-2000
		CA 2361251 A1	03-08-2000
		DE 60021700 D1	08-09-2005
		DK 1146908 T3	10-10-2005
		EP 1146908 A1	24-10-2001
		JP 2002535377 T	22-10-2002
